

Arndt
entered 2/23/05
L/Cook

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) An immunoassay method to detect a biomarker of oxidative stress in a biological sample utilizing an antibody ~~or antigen-binding fragment thereof~~ which binds said biomarker of oxidative stress, said method comprising the steps of:
 - (a) contacting a sample containing said biomarker of oxidative stress with said antibody ~~or antigen-binding fragment thereof~~ under conditions which allow binding of said biomarker of oxidative stress to said antibody ~~or antigen-binding fragment thereof~~;
 - (b) detecting the presence of said biomarker of oxidative stress in said sample.
2. (original) The method of claim 1, wherein said biological sample comprises proteins, peptides or proteineaceous aggregates.
3. (currently amended) The method of claim 1, wherein said antibody ~~or antigen-binding fragment thereof~~ is bound to a solid phase support.
4. (original) The method of claim 1 further comprising the step of:
 - (c) comparing the amount of said biomarker of oxidative stress in said sample to a control value for said biomarker of oxidative stress.
5. (original) The method of claim 1 wherein said biomarker of oxidative stress is an oxidized sulfur- or selenium-containing amino acid.
6. (original) The method of claim 5, wherein said oxidized sulfur- or selenium-containing amino acid is selected from the group consisting of the oxidation products of cysteine, cystine, methionine, selenocysteine, selenomethionine and selenocystine.

7. (original) The method of claim 5, wherein said oxidized sulfur- or selenium-containing amino acid is in a sample which comprises proteins, peptides or proteineaceous aggregates.
8. (currently amended) The method of claim 1 wherein said antibody ~~or antigen binding fragment~~ thereof is a polyclonal antibody.
9. (currently amended) The method of claim 8 wherein said polyclonal antibody detects biomarkers of oxidative stress in any protein containing said biomarkers ~~is protein nonspecific~~.
10. Cancelled
- 10 ~~11~~ ⁸ 11. (original) The method of claim ~~10~~ wherein said polyclonal antibody is specific for a protein, peptide or proteineaceous aggregate which includes an oxidized sulfur- or selenium-containing amino acid.
- 11 ~~12~~ 12. (original) The method of claim 8, wherein said polyclonal antibody is from a mouse.
- 12 ~~13~~ 13. (currently amended) The method of claim 1 wherein said antibody ~~or antigen binding fragment thereof~~ is a monoclonal antibody.
- 13 ~~14~~ ¹² 14. (currently amended) The method of claim ~~13~~ wherein said monoclonal antibody detects biomarkers of oxidative stress in any protein containing said biomarkers ~~is protein nonspecific~~.
15. Cancelled

- 13
- 14 16. (original) The method of claim 14 wherein said monoclonal antibody is specific for a protein, peptide or proteineaceous aggregate which includes an oxidized sulfur- or selenium-containing amino acid.
17. Cancelled
- 15 18. (currently amended) The method of claim 17 1, wherein said detection step comprises performing an ELISA.
- 16 19. (original) The method of claim 1 wherein picomole levels of biomarker are detected.
- 17 20. (original) The method of claim 1, wherein said sample is from an organism selected from the group consisting of: plants, bacteria, animals, viruses and fungi.
- 18 21. (original) The method of claim 20¹⁷, wherein said sample is mammalian.
- 19 22. (original) The method of claim 20¹⁷, wherein said sample is human.
- 20 23. (currently amended) A method of detecting an oxidized sulfur- or selenium-containing amino acid in a biological sample utilizing an antibody ~~or antigen-binding fragment thereof~~ which binds a protein, peptide or proteineaceous aggregate which comprises an oxidized sulfur- or selenium-containing amino acid, said method comprising the steps of:
- (a) contacting said sample with said antibody ~~or antigen-binding fragment thereof~~ under conditions which allow binding of the protein, peptide or proteineaceous aggregate and said antibody ~~or antigen-binding fragment thereof~~; and
 - (b) detecting the presence of said antibody ~~or antigen-binding fragment thereof~~ in said sample.

- 21 24. (original) The method of claim ²⁰23, wherein said biological sample comprises proteins, peptides or proteineaceous aggregates.
- 22 25. (currently amended) The method of claim ²⁰23, wherein said antibody ~~or antigen-binding fragment thereof~~ is bound to a solid phase support.
- 23 26. (original) The method of claim ²⁰23 further comprising the step of:
(c) comparing the amount of oxidized sulfur- or selenium-containing amino acid in the sample to a control value for the oxidized sulfur- or selenium-containing amino acid.
- 24 27. (original) The method of claim ²⁰23, wherein said oxidized sulfur- or selenium-containing amino acid is selected from the group consisting of the oxidation products of cysteine, cystine, methionine, selenocysteine, selenomethionine and selenocystine.
- 25 28. (original) The method of claim ²⁰23, wherein said oxidized sulfur- or selenium-containing amino acid optionally includes aggregates with other biological material comprising protein, peptides or proteineaceous aggregates.
- 26 29. (currently amended) The method of claim ²⁰23, wherein said antibody ~~or antigen-binding fragment thereof~~ is a monoclonal antibody.
- 27 30. (currently amended) The method of claim ²⁶29, wherein said monoclonal antibody detects biomarkers of oxidative stress in any protein containing said biomarkers ~~is protein nonspecific.~~
31. Cancelled

- 28 32. (original) The method of claim ²⁹31, wherein said monoclonal antibody is specific for an oxidized sulfur- or selenium-containing amino acid.
- 29 33. (currently amended) The method of claim ²⁰23, wherein said antibody ~~or antigen-binding fragment thereof~~ is a polyclonal antibody.
- 30 34. (currently amended) The method of claim ²⁹33, wherein said polyclonal antibody detects biomarkers of oxidative stress in any protein containing said biomarkers is protein nonspecific.
35. Cancelled
- 31 36. (original) The method of claim ²⁹35, wherein said polyclonal antibody is specific for an oxidized sulfur- or selenium-containing amino acid.
- 32 37. (currently amended) A method for detecting the presence of oxidative stress in an organism, said method comprising detecting the presence of an antibody ~~or antigen-binding fragment thereof~~ that binds an analyte comprising an oxidized sulfur- or selenium containing amino acid, whereby the presence of said antibody ~~or antigen-binding fragment thereof~~ is indicative of the presence of oxidative stress in said organism.
- 33 38. (original) The method of claim ³²37, wherein said organism is selected from the group consisting of: plants, bacteria, animals, viruses and fungi.
- 34 39. (original) The method of claim ³²37, wherein said organism is a mammal.
- 35 40. (original) The method of claim ³²37, wherein said organism is a human.

41. (currently amended) A method of measuring the amount of oxidative stress an organism has been exposed to, comprising:
- (a) measuring oxidized sulfur- or selenium moieties in a protein, peptide or proteineaceous aggregate from said organism;
 - (b) comparing this measurement to a control value; and determining the amount of oxidative stress the organism has been exposed to.
42. (original) The method of claim 41, wherein said organism is selected from the group consisting of: plants, bacteria, animals, viruses and fungi.
43. (original) The method of claim 42, wherein said organism is mammalian.
44. (original) The method of claim 42, wherein said organism is human.
45. (withdrawn) A method of removing oxidatively damaged protein from a sample, comprising contacting said sample with an antibody or antigen binding fragment thereof which is specific for an oxidized sulfur- or selenium-containing amino acid, whereby at least a portion of oxidatively damaged protein is bound to said antibody or antigen binding fragment thereof.
46. (withdrawn) The method of claim 45, further comprising contacting said sample with a solid support to which said antibody or antigen binding fragment thereof is attached.
47. (withdrawn) The method of claim 45, wherein said sample is selected from the group consisting of plasma, biological fluids and cells, and mixtures thereof.
48. (withdrawn) The method of claim 47, wherein said sample is plasma.
49. (withdrawn) The method of claim 48, wherein said plasma is mammalian.

50. (withdrawn) The method of claim 48, wherein said plasma is human.
51. (withdrawn) The method of claim 47, wherein said sample is biological fluids or cells.
52. (withdrawn) The method of claim 51, wherein said biological fluid or cells are mammalian.
53. (withdrawn) The method of claim 51, wherein said biological fluids or cells are human.
54. (withdrawn) A method of detecting one or more selected oxidatively damaged proteins, peptides or proteineaceous aggregates in a sample, comprising:
- (a) contacting said sample with a first antibody or antigen binding fragment thereof that binds oxidatively damaged protein, peptides or proteineaceous aggregates under conditions which allow binding of the oxidatively damaged proteins, peptides or proteineaceous aggregates with said first antibody or antigen binding fragment thereof;
 - (b) contacting said sample with a second antibody or antigen binding fragment thereof that binds a non-oxidatively damaged portion of the selected oxidatively damaged protein, peptide or proteineaceous aggregate under conditions which allow binding of the non-oxidatively damaged portion of the selected oxidatively damaged protein, peptide or proteineaceous aggregate with said second antibody or antigen binding fragment thereof;
 - (c) detecting the second antibody or antigen binding fragment thereof.
55. (withdrawn) The method of claim 54, wherein said oxidatively damaged protein, peptide or proteineaceous aggregate includes an oxidized sulfur- or selenium- containing amino acid.

56. (withdrawn) The method of claim 54, wherein said first antibody or antigen binding fragment thereof is specific for a selected oxidatively damaged protein.
57. (withdrawn) A method of determining the concentration of one or more selected oxidatively damaged proteins, peptides or proteineaceous aggregates in a sample, comprising:
- (a) contacting said sample with a first antibody or antigen binding fragment thereof that binds oxidatively damaged protein, peptides or proteineaceous aggregates under conditions which allow binding of the oxidatively damaged proteins, peptides or proteineaceous aggregates with said first antibody or antigen binding fragment thereof;
 - (b) contacting said sample with a second antibody or antigen binding fragment thereof that binds a non-oxidatively damaged portion of the selected oxidatively damaged protein, peptide or proteineaceous aggregate under conditions which allow binding of a non-oxidatively damaged portion of the selected oxidatively damaged protein, peptide or proteineaceous aggregate with said second antibody or antigen binding fragment thereof;
 - (c) measuring the amount of second antibody or antigen binding fragment thereof in the sample.
58. (withdrawn) The method of claim 57, wherein said oxidatively damaged protein, peptide or proteineaceous aggregate contains an oxidized sulfur- or selenium-containing amino acid.
59. (withdrawn) The method of claim 57, wherein said first antibody or antigen binding fragment thereof is specific for a selected oxidatively damaged protein, peptide or proteineaceous aggregate.

60. (withdrawn) A method for detecting or diagnosing the presence of a disease associated with oxidative stress in a mammalian subject comprising:
- (a) evaluating the level of biomarker of oxidative stress in a biological sample from a mammalian subject according to claim 4; and
 - (b) comparing the level detected in step (a) to a level of biomarker of oxidative stress normally present in the mammalian subject;
- wherein an increase in the level of biomarker for oxidative stress as compared to normal levels indicates a disease associated with elevated levels of biomarker of oxidative stress.
61. (withdrawn) A method for monitoring the course of a disease associated with elevated levels of biomarker of oxidative stress in a mammalian subject comprising evaluating the level of biomarker of oxidative stress in a series of biological samples obtained at different time points from a mammalian subject according to the method of claim 4, wherein an increase in the level of biomarker of oxidative stress over time indicates progression of the disease, and wherein a decrease in the level of biomarker of oxidative stress over time indicates regression of the disease.
62. (withdrawn) A method for monitoring a therapeutic treatment of a disease associated with elevated levels of biomarker of oxidative stress comprising evaluating the level of biomarker of oxidative stress in a series of biological samples obtained at different time points from a mammalian subject undergoing a therapeutic treatment for a disease associated with elevated levels of biomarker of oxidative stress according to the method of claim 4, wherein a decrease in the level of biomarker of oxidative stress over time indicates an effective therapeutic outcome.
63. (withdrawn) A monoclonal antibody which binds a biomarker of oxidative stress.

64. (withdrawn) The monoclonal antibody of claim 63, wherein said biomarker of oxidative stress is a protein, peptide or any proteineaceous aggregate containing an oxidized sulfur- or selenium-containing amino acid.
65. (withdrawn) The monoclonal antibody of claim 63, wherein said monoclonal antibody is produced by hybridoma cell line K2.F1.
66. (withdrawn) The hybridoma cell line K2.F1.6 deposited with the American Type Culture Collection (ATCC).
67. (withdrawn) A monoclonal antibody which binds proteins, peptides or proteineaceous aggregates containing oxidized sulfur- or selenium-containing amino acids.
68. (withdrawn) A polyclonal antibody which binds a biomarker of oxidative stress.
69. (withdrawn) The polyclonal antibody of claim 68, wherein said biomarker of oxidative stress is a protein, peptide or proteineaceous aggregate containing an oxidized sulfur- or selenium-containing amino acid.
70. (withdrawn) A polyclonal antibody which binds proteins, peptides or proteineaceous aggregates containing oxidized sulfur- or selenium-containing amino acids.
71. (withdrawn) A monoclonal antibody preparation wherein the monoclonal antibody is specific for oxidized sulfur- or selenium-containing amino acids in a protein, peptide or proteineaceous aggregate.
72. (withdrawn) The monoclonal antibody preparation of claim 71, wherein said monoclonal antibody is produced by hybridoma cell line K2.F1.

73. (withdrawn) A polyclonal antibody preparation wherein the polyclonal antibody is specific for oxidized sulfur- or selenium-containing amino acids in a protein, peptide or proteineaceous aggregate.
74. (withdrawn) The polyclonal antibody preparation of claim 73, wherein said polyclonal antibody is produced by an animal capable of producing the polyclonal antibody preparation.
75. (withdrawn) The polyclonal antibody preparation of claim 74, wherein said animal is selected from the group consisting of mouse, rat, rabbit, chicken and goat.
76. (withdrawn) A hybridoma cell line producing a monoclonal antibody specific for oxidized sulfur- or selenium containing amino acids in a protein or proteineaceous aggregate.
77. (withdrawn) The hybridoma cell line of claim 76 which is K2.F1.
78. (withdrawn) The hybridoma cell line of claim 77 which is K2.F1.6.
79. (withdrawn) A test kit for measuring the presence of oxidative damage in an analyte, comprising an antibody or an antigen binding fragment thereof, which antibody or antigen binding fragment is an antibody or antigen binding fragment thereof specific for a protein, peptide or proteineaceous aggregate which contains an oxidized sulfur- or selenium-containing amino acid.
80. (withdrawn) A method for preparing a polyclonal antibody against a specific disease associated with an oxidized sulfur- or selenium-containing amino acid comprising:
 - (a) obtaining a sample from an organism having a selected disease;

- (b) preparing a polyclonal antibody directed against the selected disease from said sample.
81. (withdrawn) The method of claim 80 wherein said selected disease is selected from the group consisting of coronary artery disease, renal disease and diabetes.
82. (new) The method of claim 1, wherein the antibody is produced by hybridoma cell line K2.F1.
83. (new) The method of claim 23, wherein the antibody is produced by hybridoma cell line K2.F1.
84. (new) The method of claim 37, wherein the antibody is produced by hybridoma cell line K2.F1.